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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PC26214A		FOR FURTHER ACTION		See Form PCT/PEA/416
International application No. PCT/IB2004/003815		International filing date (day/month/year) 22.11.2004	Priority date (day/month/year) 02.12.2003	
International Patent Classification (IPC) or national classification and IPC C07D205/04, C07B43/08				
Applicant PFIZER PRODUCTS INC. et al.				
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau) a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>				
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input checked="" type="checkbox"/> Box No. VIII Certain observations on the international application</p>				
Date of submission of the demand 17.12.2004		Date of completion of this report 25.10.2005		
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer Bérillon, L Telephone No. +49 89 2399-		



**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/IB2004/003815

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-11 as originally filed

Claims, Numbers

1-7 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing *(specify)*:
 - ☐ any table(s) related to sequence listing *(specify)*:
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing *(specify)*:
 - ☐ any table(s) related to sequence listing *(specify)*:

* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/IB2004/003815

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-7
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-7
Industrial applicability (IA)	Yes: Claims	1-7
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 Prior art

Reference is made to the following documents:

- D1: US-A-3 155 669
- D2: DE 44 05 178
- D3: TETRAHEDRON vol. 55, no. 24, p. 7625-7644
- D4: J. MED. CHEM., vol. 39, 1996, p. 3169-3173
- D5: J. MED. CHEM., vol. 41, 1998, p. 5084-5093
- D6: BIOORGANIC & MEDICINAL CHEMISTRY LETTERS vol. 9, no.16, p. 2343-2348
- D7: BULL. CHEM. SOC. JPN., vol. 54, 1981, pages 793-799

2 Novelty (Article 33(2) PCT)

The present process consists of the following steps:

- step 1 (IA gives IB): formation of an alpha amino cyano group
- step 2 (IB gives IC): hydrolysis of the cyano group with alkaline hydrogen peroxide in DMSO
- step 3 (IC gives I): deprotection step

Although D1-D6 disclose said step 1 or closely related reactions, they miss present step 2.

D7 discloses the hydrolysis of a cyano group with alkaline hydrogen peroxide in DMSO but misses present step 1.

Hence, novelty is acknowledged for the present application.

3 Inventive step (Article 33(3) PCT)

The technical problem underlying the present application is regarded as the provision of a process for the preparation of compounds of formula (I) (see present claim 1). The claimed process relates to a modification of the Strecker synthesis (conversion of aldehydes or ketones into the corresponding alpha amino acid derivatives). The Strecker synthesis is used for example in D2, D4 and D5 using a starting material similar to that of the present application (see D2, page 8, scheme 5; D4, page 3170, scheme 1, steps a and b; D5, page 5086, scheme 1, steps a and b). The claimed process appears to differ from D2, D4 and D5 in view of the hydrolysis of the cyano group (step 2) which is performed with alkaline hydrogen peroxide in DMSO (cited prior art D2, D4 and D5 use a mineral acid such as H_2SO_4 instead). It is noted however that such a hydrolysis of a cyano group is already known in the prior art (see D7) and therefore cannot establish inventive step for the present process. No technical feature of step 1 appear to establish inventive step either.

Re Item VIII

Certain observations on the international application

In claim 1 an amine is mentioned as reagent ($R^{4d}-NH-R^{4d'}$) whereas in example 1 an amine salt is used (ethylamine hydrochloride). This inconsistency raises doubts as to the exact claimed scope.